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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,012	01/19/2001	Torben Halkier	3631-0104P	3059

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EXAMINER

VOGEL, NANCY S

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/744,012

Applicant(s)

HALKIER ET AL

Examiner

Nancy Vogel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 19 January 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-53 is/are pending in the application.
- 4a) Of the above claim(s) 41-53 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-40 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-40, drawn to a method for identifying a modulator.

Group II, claim(s) 41-43, drawn to a method of preparing an expression vector for expressing a modulator, a method of preparing a transformed cell for expressing a modulator, and a method of preparing a modulating using the transformed cell and expression vector.

Group III, claim(s) 44-49, drawn to a method of isolating an/or identifying a target biomolecule.

Group IV, claim(s) 50-51, drawn to a method for selecting a chemical compound as a putative drug candidate.

Group V, claim(s) 52, drawn to a method for the preparation of a medicinal product.

Group VI, claim(s) 53, drawn to a method for developing a medicinal product.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

PCT Rule 13.2 requires that unity of invention exists only when the shared same or corresponding technical feature is a contribution over the prior art. The inventions listed as Groups I-V do not relate to a single general inventive concept because they lack the same or corresponding special technical feature. The "special technical feature" of Groups I-V is the randomly modified nucleotide sequence derived from a parent nucleotide sequence encoding a parent peptide which in vivo directly modulates activity of a known protease, comprising an invariable part serving to stabilize a polypeptide

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fragment and being stable towards proteolytic attack and/or being insensitive to a reducing environment, and random nucleotides which is shown by Roberts et al., Rottgen et al., Jespers et al., Dennis et al. and Markland et al. Each of these references disclose randomized sequences introduced into protease inhibitors. Roberts et al. disclose bovine pancreas trypsin inhibitor,

During a telephone conversation with Mr. Leonard Svensson on August 21, 2003 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-40. Affirmation of this election must be made by applicant in replying to this Office action. Claims 41-53 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of identifying a modulator which is a polypeptide fragment, wherein a pool of expression vectors are constructed having a) a parent nucleotide sequence which encodes a protein that modulates activity of a known protease as an scaffold protein, wherein said scaffold portion stabilizes said polypeptide fragment, and being stable towards proteolytic attack and/or being insensitive to a reducing environment, and b) random nucleotides. The claims are genus claims in terms of a method of identifying a modulator using any protease modulator, or a fragment of said protease modulator, or a part of a protease inhibitor listed in claims 21-23, which would stabilize the polypeptide encoded by random nucleotides inserted into the coding sequence of said protease modulators in vivo in any cell. The specification teaches the method using the full length protease inhibitor barley chymotrypsin inhibitor 2A (CI-2A). The disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all the methods utilizing the encompassed proteins that modulates activity of a known polypeptides based on the teachings of the specification. While the specification provides lists of protease inhibitors (pages 40-58 of the specification), there is no disclosure of which of the fusion partners would, when utilized in the vector recited in the claims, provide stability to the polypeptides encoded by random nucleotides, and have the properties of "being stable towards proteolytic attack and/or being insensitive to a reducing environment" in any particular cell environment. There is

no assay disclosed in the specification to show that the protease modulator "stabilizes" the random nucleotide or renders the fusion protein stable towards any particular proteolytic attack and/or insensitive to a reducing environment, and it is not clear how one would determine these properties. There is no disclosure of which portion or fragment of any protease modulator would possess the recited properties.

Furthermore, there is no structure-function analysis of modulators of proteases, which the specification defines as enhancers or inhibitors of said proteases, to provide guidance on modulators which could be used as scaffolds for random nucleotides, such that said nucleotides would be stabilized in the interior of any host cell. Such factors as where in the modulators the random nucleotides should be located in the numerous possible scaffold proteins which "modulate" a known protease, such that the polypeptide fragment encoded by the random nucleotides are "stabilized" and the fusion protein is "stable towards proteolytic attack and/or being insensitive to a reducing environment" are not disclosed. Therefore, the specification does not describe the claimed method utilizing modulators of a known protease as scaffold proteins for a polypeptide encoded by a random polynucleotide in such full, clear, concise and exact terms so as to indicate that applicant has possession of the method at the time of filing the present application. Thus, the written description requirement has not been satisfied.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, and by dependence, claims 2-40 are vague and indefinite in the term "derived from" since it is not clear what this encompasses.

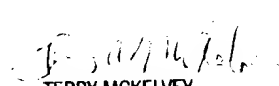
Claim 1, and by dependence, claims 2-40 are vague and indefinite in the term "known protease", since it does not clearly recite what proteases are intended.

Claim 1, and by dependence, claims 2-40 are vague and indefinite in the term "serving to stabilize said polypeptide fragment" since it is not clear what is intended. Does applicant intend that the polypeptide fragment has a longer half-life as compared to the polypeptide fragment alone in the interior of a host cell, or that it is constrained in a particular three-dimensional position, or something else?

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy Vogel whose telephone number is (703) 308-4548. The examiner can normally be reached on 7:30 - 4:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


TERRY MCKELVEY
PRIMARY EXAMINER